

Bacteremic complications of intravascular catheter tip colonization with Gram-negative micro-organisms in patients without preceding bacteremia

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Abstract Although Gram-negative micro-organisms are frequently associated with catheter-related bloodstream infections, the prognostic value and clinical implication of a positive catheter tip culture with Gram-negative micro-organisms without preceding bacteremia remains unclear. We determined the outcomes of patients with intravascular catheters colonized with these micro-organisms, without preceding positive blood cultures, and identified risk factors for the development of subsequent Gram-negative bacteremia. All patients with positive intravascular catheter tip cultures with Gram-negative micro-organisms at the University Medical Center, Utrecht, The Netherlands, between 2005 and 2009, were retrospectively studied. Patients with Gram-negative bacteremia within 48 h before catheter removal were excluded. The main outcome measure was bacteremia with Gram-negative micro-organisms. Other endpoints were length of the hospital stay, in-hospital mortality, secondary complications of Gram-negative bacteremia, and duration of intensive care admission. A total of 280 catheters from 248 patients

were colonized with Gram-negative micro-organisms. Sixty-seven cases were excluded because of preceding positive blood cultures, leaving 213 catheter tips from 181 patients for analysis. In 40 (19%) cases, subsequent Gram-negative bacteremia developed. In multivariate analysis, arterial catheters were independently associated with subsequent Gram-negative bacteremia (odds ratio [OR]=5.00, 95% confidence interval [CI]: 1.20–20.92), as was selective decontamination of the digestive tract (SDD) (OR=2.47, 95% CI: 1.07–5.69). Gram-negative bacteremia in patients who received SDD was predominantly caused by cefotaxime (part of the SDD)-resistant organisms. Mortality was significantly higher in the group with subsequent Gram-negative bacteremia (35% versus 20%, OR=2.12, 95% CI: 1.00–4.49). Patients with a catheter tip colonized with Gram-negative micro-organisms had a high chance of subsequent Gram-negative bacteremia from any cause. This may be clinically relevant, as starting antibiotic treatment pre-emptively in high-risk patients with Gram-negative micro-organisms cultured from arterial intravenous catheters may be beneficial.

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Introduction

Intravascular catheters are a significant source of bloodstream infections in hospitalized patients [1–3]. In Europe, the overall incidence of nosocomial bloodstream infections is five episodes per 1,000 days of in situ central venous catheter (CVC). [3]. Gram-negative micro-organisms are commonly associated with such catheter-related bloodstream infections, with up to 32% of the bloodstream infections in intensive care units (ICU) being caused by Gram-negative micro-organisms [2, 4, 5]. *Escherichia coli*,

Klebsiella species, and, in ICUs, *Enterobacter* species are most commonly isolated [1, 3, 4]. The case–fatality ratios of Gram-negative bloodstream infections are high and range between 9 and 28% [1], with one study even reporting an overall mortality of 35% [5]. Although Gram-negative bloodstream infections are frequently associated with catheter tip colonization, the prognostic value and clinical implication of a positive catheter tip culture without preceding Gram-negative bacteremia remains unclear [2, 6]. Recent studies show that 12 to 24% of patients with *Staphylococcus aureus* colonization of an intravascular catheter develop subsequent bacteremia, especially if they did not receive effective antibiotics within 24 to 48 h after catheter removal [7, 8]. Currently, it is common practice to pre-emptively treat *S. aureus*-colonized catheter tips.

For Gram-negative micro-organisms, the guidelines for the management of intravascular catheter-related infections give no specific advice on the appropriate management in the case of a positive catheter tip culture with Gram-negative micro-organisms, without preceding bacteremia, due to a lack of literature on this subject [2, 6].

Therefore, the aim of this study was to determine the outcomes of patients with intravascular catheters that were colonized with Gram-negative micro-organisms, without positive blood cultures in a 48-h period before catheter removal, and to identify the risk factors for the development of a subsequent bacteremia.

Methods

Study design and patient population

This retrospective study was conducted at the University Medical Center Utrecht, a tertiary care hospital with 1,042 beds, situated in the Netherlands. Patients whose intravascular catheter tips had been cultured between January 1, 2005 and July 1, 2009 were selected from the electronic database of the bacteriology department (GLIMS version 7.2.4). We selected catheter tip cultures positive for Gram-negative micro-organisms. Patients with one or more positive blood cultures with Gram-negative micro-organisms in the period up to 48 h before the removal of the intravascular catheter were excluded. All blood cultures, conducted in the period from 30 days to 2 days before catheter removal and the period of 90 days after catheter removal, were recorded, along with all other positive cultures with Gram-negative micro-organisms in the same period. We chose a time frame of 48 h because we assumed that, in bacteremic patients with persistent foci and systemic inflammatory response syndrome (SIRS), they would have positive blood cultures. Possible risk factors for Gram-negative bacteremia, including admission to the ICU, mechanical ventilation, malignancy, stem cell and solid organ

transplantation, liver failure, diabetes, pulmonary disease, hemodialysis, neutropenia, and treatment with immunosuppressive medication, were recorded.

The use of antibiotics in a period of 14 days around catheter removal and the administration of selective decontamination of the digestive tract (SDD) were recorded. Since April 2008, SDD is given to the ICU patients in our institution. It consists of the local application of polymyxin E, tobramycin, and amphotericin B in the oropharynx and administration to the stomach with a nasogastric tube until discharge from the ICU. Local administration is combined with intravenous cefotaxime for 4 days [9].

Outcome measures

The main outcome measure was subsequent bacteremia with Gram-negative micro-organisms, which was defined as at least one positive blood culture, taken within 90 days after the removal of the intravascular catheter, with an isolate identical (i.e., the same species and genera type and the same antibiotic resistance pattern) to that of the catheter tip. The blood culture (s) had to become positive later than the catheter tip culture. If multiple Gram-negative micro-organisms were present on a catheter tip, these all had to be found in a blood culture in order to conclude that there was a subsequent bacteremia. Secondary endpoints were the duration of hospital stay, in-hospital mortality, complications (cerebrovascular accident, endocarditis, septic spreading, or a combination of these), and duration of intensive care admission.

Catheter exit site infections and SIRS, at the time of catheter removal, was also recorded. A catheter exit site infection was defined as one of the following clinical signs at the time of catheter removal: tenderness, induration, erythema, purulence, or obstruction of the catheter [6]. SIRS was defined as two or more of the following manifestations: a body temperature $<36^{\circ}\text{C}$ or $>38^{\circ}\text{C}$, a heart rate >90 beats per minute, tachypnea with a respiratory rate >20 breaths per minute, or an arterial partial CO_2 pressure <4.3 kPa, and a white blood cell count $>12,000$ cells/ mm^3 or $<4,000$ cells/ mm^3 or the presence of more than 10% immature neutrophils [10].

Culture technique

The catheter tips were processed as described elsewhere [11]. Blood cultures were incubated for a minimum of 5 days at 35°C .

Statistical analysis

The data were analyzed using SPSS 15.0 for Windows. Student's *t*-test was used for normally distributed continuous variables and the Mann–Whitney *U*-test for continuous

variables with a non-parametric distribution. For nominal variables, we used the Pearson Chi-square test, Fisher's exact test, and the likelihood ratio. The results of the continuous variables are expressed as means with standard deviations (SDs) or medians with interquartile ranges (IQRs), and the nominal variables as the number of cases with percentages. Variables with a two-sided p -value of ≤ 0.05 were considered to be significant. All predictors with a pathophysiological correlation or showing an association with $p < 0.15$ in the univariate analysis were selected for multivariate logistic regression analysis. Subsequently, we used the risk factors with $p \leq 0.05$ (Table 1), which were independently associated with the development of a Gram-negative bacteremia, to construct a logistic regression model to analyze potential interactions. Missing values were excluded from the univariate and multivariate analysis.

Results

Between January 2005 and July 2009, 213 catheter tips (further referred to as cases) from 181 patients (mean age 52 years, 135 males) were positive for Gram-negative micro-organisms. Of those, in 40 cases (19%) a subsequent Gram-negative bacteremia developed. Blood cultures performed after the removal of the intravascular catheter were available in 162 (76%) of the cases. The median time from the removal of the intravascular catheter to demonstrated bacteremia was 4 days (IQR: 3–9 days). There were no positive blood cultures with the same micro-organism after 10 days following catheter removal. The patient demographics and differences in characteristics between patients with and without bacteremia are summarized in Table 1.

An exit site infection was present in 37 cases (17%), but was not significantly different between the groups. In 86% of the cases, antibiotic treatment had already been prescribed in a period of 14 days around catheter removal. Ninety-six percent of cases with SIRS at the time of removal of the intravascular catheter was treated with antibiotics, compared to 87% of the cases without SIRS ($p = 0.02$). Mortality was significantly higher in cases with subsequent Gram-negative bacteremia compared to cases without a Gram-negative bacteremia (35% vs. 20%, OR = 2.12, 95% CI: 1.00–4.49).

The Gram-negative micro-organisms most frequently cultured from the removed catheter tips were *Enterobacter cloacae* (21%), *Pseudomonas aeruginosa* (17%), and *Klebsiella pneumoniae* (13%) (Table 2). Twenty-nine catheter tips (14%) contained multiple Gram-negative micro-organisms. On 67 catheter tips (31%), micro-organisms other than Gram-negative bacteria were present, of which coagulase-negative *Staphylococcus* was the most frequently isolated organism (22%) (Table 2). To evaluate whether a majority of patients already had bacteremia even before the 48 h before

catheter removal, we also analyzed whether positive blood cultures were present from 30 days to 48 h before catheter removal with the same Gram-negative micro-organism as that ultimately found on the catheter tip. An additional 16 cases (7.5%) were identified which had positive blood cultures with the same micro-organism in this period but not within 48 h before catheter removal.

Risk factors for subsequent Gram-negative bacteremia

In the multivariate logistic regression analysis, localization of the intravascular catheter in an artery ($p = 0.048$, OR = 3.67, 95% CI: 1.01–13.26) and the administration of SDD ($p = 0.033$, OR = 2.47, 95% CI: 1.07–5.69) were associated with the development of subsequent Gram-negative bacteremia (Table 3). The constructed model adequately predicted the variables with a significance of 0.014, which was confirmed by the Hosmer–Lemeshow test ($p = 0.78$). The constant factor had a p -value < 0.001 .

Discussion

Our study suggests that an intravascular catheter tip colonized with Gram-negative micro-organisms is an early indicator of subsequent Gram-negative bacteremia in 19% of cases. Only one previous study has investigated positive intravenous line tip cultures as predictors for bacteremia [12]. In that study, an intravascular catheter tip colonized with Enterobacteriaceae and *Pseudomonas* species was predictive of subsequent Gram-negative bacteremia in 20 and 14% of the cases, respectively. Although their sample size was relatively small (74 patients with Enterobacteriaceae, 22 patients with *Pseudomonas* species on the catheter), these results seem to be comparable with our results [12].

In the univariate analysis, several risk factors were associated with the development of Gram-negative bacteremia in our study. In the multivariate analysis, patients with a positive culture of an arterial catheter were almost four times more likely to develop subsequent Gram-negative bacteremia. Several other studies have investigated the association between the catheter site and the development of a catheter-related bacteremia [13–15]. Deshpande et al. found no significant difference in the central venous catheter infections between subclavian, internal jugular, and femoral catheters [14]. The study conducted by Lorente et al. showed that jugular catheters are safer than femoral catheters concerning the risk of a catheter-related bacteremia [13] and Nagashima et al. concluded that subclavian catheters, in turn, are less frequently associated with a catheter-related bacteremia than jugular catheters [15]. Based on these findings, the guidelines regarding the prevention of intravascular catheter-related infections of

Table 1 Characteristics of the 213 cases with intravascular catheter tips colonized with Gram-negative micro-organisms in 181 patients

	No subsequent GNB (<i>n</i> =173)	Subsequent GNB (<i>n</i> =40)	<i>p</i> -value	OR of difference (95% CI), univariate analysis
Age, mean years ± SD	52±23	54±27	0.61	-2.12 (-10.3–6.1)
Male gender	112 (65)	23 (58)	0.39	1.4 (0.65–3.16)
Ward				
Internal medicine	23 (13)	3 (8)	0.31	0.53 (0.15–1.86)
Surgical	58 (34)	16 (40)	0.44	1.32 (0.62–2.68)
Intensive care	9 (5)	0 (0)	0.14	0.98 (0.92–0.98)
Neurology	23 (13)	2 (5)	0.14	0.34 (0.08–1.52)
Cardiology	27 (16)	10 (25)	0.16	1.80 (0.79–4.11)
Pediatrics	17 (10)	6 (15)	0.34	1.61 (0.60–4.41)
Outpatient	3 (2)	1 (3)	0.75	1.45 (0.15–14.35)
Other	13 (8)	2 (5)	0.58	0.65 (0.14–3.00)
Co-morbid condition				
Organ transplantation	2 (1)	1 (3)	0.74	2.19 (0.19–24.79)
Stem cell transplantation	3 (2)	1 (3)	0.49	1.45 (0.15–14.35)
Liver failure	4 (2)	0 (0)	0.33	0.97 (0.96–1.0)
COPD	14 (8)	2 (5)	0.76	0.60 (0.13–2.74)
Hemodialysis	23 (13)	7 (18)	0.58	1.38 (0.54–3.49)
Malignancy	54 (31)	10 (25)	0.85	0.74 (0.34–1.61)
Abdominal surgery	69 (40)	17 (43)	0.29	1.11 (0.56–2.24)
Diabetes mellitus	21 (12)	3 (8)	1	0.59 (0.17–2.07)
Cardiovascular disease	72 (42)	16 (40)		0.94 (0.46–1.89)
Immunosuppressive medication	129 (75)	33 (83)	0.05	0.38 (0.14–1.04)
Urgency indication for the placement of an intravascular catheter	8 (5)	2 (5)	0.89	1.12 (0.22–560)
Length of hospital stay until catheter removal, median days (IQR)*	15 (8–35)	30 (14–60)	0.017	–
Length of ICU stay until catheter removal, median days (IQR)	8 (0–24)	17 (3–37)	0.081	–
Ventilation	125 (72)	33 (83)	0.18	1.81 (0.75–4.37)
Duration of ventilation until catheter removal, median days (IQR)	7 (0–21)	17 (2–32)	0.07	–
Duration of intravascular catheter in situ, median days (IQR)	9 (0–34)	10 (6–18)	0.75	–
Localization of intravascular catheter				
Jugular vein*	51 (30)	5 (13)	0.05	0.38 (0.14–1.04)
Subclavian vein	41 (24)	10 (25)	0.61	1.2 (0.55–2.81)
Femoral vein	55 (32)	12 (30)	0.86	1.07 (0.49–2.32)
Umbilical vein	1 (1)	0 (0)	1	1.0 (0.98–1.06)
Artery*	8 (5)	7 (18)	0.006	5.02 (1.68–14.99)
Peripheral	7 (4)	0 (0)	0.61	0.96 (0.93–0.99)
Type of intravascular catheter*				
Standard	125 (72)	27 (68)	0.56	0.80 (0.38–1.67)
PICC	4 (2)	5 (13)	0.04	6.04 (1.54–23.62)
Tunneled	8 (5)	3 (8)	0.46	1.67 (0.42–6.61)
Catheter exit site infection ^a	34 (20)	3 (8)	0.12	0.38 (0.11–1.35)
SIRS	67 (39)	14 (35)	0.40	0.73 (0.36–1.51)
Antibiotic treatment ^b	147 (85)	37 (93)	0.085	5.54 (0.72–42.42)
Appropriate antibiotic treatment 24 h before to 48 h after catheter tip culture	58 (34)	16 (40)	0.44	1.32 (0.65–2.68)
Antibiotic treatment not appropriate 24 h before to 48 h after catheter tip culture	89 (51)	21 (53)	0.9	1.04 (0.52–2.08)

Table 1 (continued)

	No subsequent GNB (<i>n</i> =173)	Subsequent GNB (<i>n</i> =40)	<i>p</i> -value	OR of difference (95% CI), univariate analysis
No antibiotic treatment 24 h before to 48 h after catheter tip culture	26 (15)	3 (8)	0.21	0.45 (0.13–1.60)
SDD*	33 (19)	15 (38)	0.012	2.55 (1.21–5.36)
Of these, cultured organism sensitive to cefotaxime	2 (1)	1 (3)	1	–
Albumin (g/L), mean±SD ^c	22.0±7.5	18.5±7.1	0.076	3.50 (–0.37–7.37)
Neutrophils (×10 ⁹ /L), mean±SD ^d	10.2±6.0	11.2±6.4	0.6	–1.03 (–4.89–2.83)
Neutropenia (neutrophils<1.6×10 ⁹ /L)	2 (1)	1 (3)	0.46	2.32 (0.19–27.89)

Nominal variables are expressed as the number of cases along with percentages, and continuous variables as means with standard deviations (SDs) or medians with interquartile ranges (IQRs). Variables with a *p*-value of ≤0.05 were considered to be significant, and variables with *p*≤0.05 that were associated with the development of a Gram-negative bacteremia were included in the multivariate analysis

GNB, Gram-negative bacteremia; OR, odds ratio of the univariate analysis; CI, confidence interval; *n*, number of cases; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; PICC, peripherally inserted central catheter; SIRS, systemic inflammatory response syndrome; SDD, selective decontamination of the digestive tract (polymyxin E/tobramycin/amphotericin B/cefotaxime)

*These risk factors are included in the multivariate logistic regression analysis

^a Signs of exit site infection in patients without GNB were pain (*n*=3), swelling (*n*=7), redness (*n*=26), purulence (*n*=12), and blockage of catheter (*n*=1). Signs of exit site infection in patients with GNB were redness (*n*=2) and purulence (*n*=1)

^b Antibiotic treatment in a period of 2 weeks before until 2 weeks after catheter removal

^c Albumin level in a period of 1 week before until 1 week after catheter removal

^d Neutrophils level on the day of catheter removal, 1 day after, or 1 day before catheter removal

the Centers for Disease Control and Prevention (CDC) recommend the use of a subclavian site (rather than a jugular or femoral site) to minimize the risk of catheter-related infection [16]. The higher incidence of Gram-negative bacteremia in patients with an arterial catheter could be explained by the fact that most of the catheters were located in the femoral artery and the groin is considered to be a contaminated area [17, 18].

The multivariate analysis also showed that patients who received SDD during their admission to the ICU were almost 2.5 times more likely to develop subsequent Gram-negative bacteremia. Silvestri et al. conducted a systemic review of randomized, controlled trials regarding the effect of SDD on bacterial bloodstream infections in critically ill patients [19]. They concluded that SDD significantly reduces Gram-negative bacteremia, with an odds ratio of 0.39 [19]. However, a recent study conducted by Oostdijk et al. has showed that SDD leads to resistant microorganisms [20], which can complicate antibiotic treatment and may result in a greater risk of developing subsequent Gram-negative bacteremia. In our study, Gram-negative bacteremia in patients who received SDD was associated with cefotaxime-resistant organisms.

Furthermore, the outcome variables were affected by the presence of Gram-negative bacteremia. Patients with catheter tips colonized with Gram-negative bacteria had a 35% mortality as compared to 20% among those without Gram-negative bacteria on the removed catheter tip. The

mortality found in our study is relatively high compared to some other studies [1], but is comparable to the study conducted by Crowe et al. between 1985 and 1996 [5]. Compared to other studies, there also is a difference in the type of Gram-negative micro-organism found on the catheter tips. Previous studies found *E. coli*, *Klebsiella* species, and, in ICUs, *Enterobacter* species as the most important micro-organisms on intravascular catheter tips [1, 3, 4]. We found *E. cloacae* on most of the catheter tips, followed by *P. aeruginosa* and *K. pneumoniae*. The difference might be explained by the fact that the majority of our patients (78%) was admitted to the ICU and *Enterobacter* species are common Gram-negative micro-organisms in the ICU [4].

A limitation of our study is that it might underestimate the association between catheter tip colonization and the subsequent development of a Gram-negative bacteremia because blood cultures as a test for bacteremia are not 100% sensitive. Further limitations are the retrospective study design and the inherent possibility of patient prescription bias. There was, for example, no clear protocol on the prescription of antibiotics at the time of removal of the intravascular catheter, except for the ICU patients who received SDD during their ICU admission. In our institution, the end of treatment, fever, unexplained leukocytosis or inflammatory markers, and exit site infections are reasons for catheter extraction. Catheter tips are routinely sent for culture in ICU patients and in other wards in case

Table 2 Overview of Gram-negative and other micro-organisms on 213 catheter tips

	No subsequent GNB (<i>n</i> =173)	Subsequent GNB (<i>n</i> =40)	<i>p</i> -value	OR (95% CI)
Type of GNM on catheter tip				
<i>Enterobacter</i> species	35 (20)	16 (40)	0.08	2.63 (1.26–5.47)
<i>Escherichia coli</i>	19 (11)	5 (13)	0.89	1.09 (0.34–3.15)
<i>Klebsiella</i> species	32 (18)	8 (20)	0.76	1.15 (0.48–2.72)
<i>Morganella morganii</i>	10 (6)	2 (5)	0.84	0.86 (1.18–4.08)
<i>Proteus</i> species	17 (10)	2 (5)	0.33	0.48 (0.11–2.18)
<i>Pseudomonas</i> species	31 (18)	10 (25)	0.31	1.53 (0.68–3.45)
<i>Serratia</i> species	10 (6)	1 (3)	0.4	0.40 (0.05–3.36)
<i>Stenotrophomonas maltophilia</i>	11 (6)	1 (3)	0.34	0.38 (0.05–3.01)
Other ^a	11 (6)	0 (0)		
Multiple GNM on the catheter tip	23 (13)	6 (15)	0.78	1.15 (0.43–3.04)
Other micro-organisms on the catheter tip	53 (31)	14 (35)	0.59	1.22 (0.59–2.52)
Types of other micro-organisms				
<i>Candida</i> species	2 (1)	0 (0)		
CNS	37 (21)	9 (23)		
<i>Corynebacterium</i> species	4 (2)	0 (0)		
<i>Enterococcus</i> species	11 (6)	2 (5)		
<i>Staphylococcus aureus</i>	7 (4)	4 (10)		

Variables are expressed as the number of cases along with percentages

GNB, Gram-negative bacteremia (with isolates identical to that of the catheter tip); *n*, number of cases; GNM, Gram-negative micro-organisms; CNS, coagulase-negative *Staphylococcus*

^aOther GNM: *Acinetobacter* species, *Achromobacter* species, *Chryseobacterium indologenes*, *Citrobacter* species, *Moraxella catarrhalis*, *Providencia rettgeri*, *Pantoea agglomerans*

of the suspicion of catheter-related sepsis. Unfortunately, we have no data on the exact reason for culturing the catheter tips in individual cases. Treatment of a patient after the result of the culture became available was left at the discretion of the treating physician. In the case of residing fever and decrease of inflammatory markers, antibiotic treatment may be withheld in individual cases. The coincidence of bacteremia with catheter tip colonization may be explained by several mechanisms. First, colonization of the catheter after previous bacteremia for any reason. If we assume, however, that severe sepsis was present in the 48 h before catheter removal, blood cultures taken during those 48 h would likely have become positive. However, 7.5% of patients had bacteremia before 48 h before catheter removal and not within the time frame of 48 h before catheter removal. Due to the retrospective nature of our study, the interpretations of these findings are dependent on the availability of information, on the

practices of clinicians, and may be blurred by previous antibiotic treatment around catheter removal. Second, contamination of the catheter tip after the removal of the catheter (e.g., contamination in the laboratory). This is highly unlikely in patients who develop subsequent bacteremia. Third, bacteremia after the colonization of the catheter whilst in situ. This is the most likely pathophysiological mechanism if the catheter itself is the source of bacteremia. Fourth, if a persistent focus for bacteremia exists and the line is extracted for suspected catheter infection. This hypothesis might be supported by the lack of an observed effect of antibiotic treatment on subsequent bacteremia. Unfortunately, due to the retrospective nature of our study, we have no data on the exact reasons for catheter removal or persistent foci. However, this observation urges for follow up blood cultures or investigations to identify persistent foci if Gram-negative bacteremias are found on extracted catheters.

Table 3 Results of the multivariate analysis of factors associated with subsequent Gram-negative bacteremia

	Odds ratio	95% CI
Having received SDD	2.47	1.07–5.69
Localization of the catheter in an artery	3.67	1.01–13.26

Factors included in the multivariate analysis were: duration of hospital admission before catheter removal, localization of the catheter in an artery, localization of the catheter in the femoral vein, received SDD, and the type of catheter

The strength of this study is that a large number of positive catheter tips were included, with a high incidence of subsequent bacteremia. All cases in the time frame eligible for inclusion were most likely to be identified in the digital database. This enabled us to calculate results with a relatively large statistical power. However, this remains a retrospective study and larger prospective studies are required in order to further substantiate our results.

Due to the lack of evidence, the guidelines for the management of intravascular catheter-related infections have given no specific advice on the appropriate manage-

ment in the case of a positive catheter tip culture with Gram-negative micro-organisms without preceding bacteremia [2, 6]. Based on our results, it is suggested that an intravascular catheter tip colonized with Gram-negative micro-organisms is predictive of subsequent Gram-negative bacteremia in 19% of cases. Also, a Gram-negative bacteremia seems to be associated with the placement of a catheter in a femoral artery. The mortality has to be further explored, because it is not clear what other factors may have been of influence. In conclusion, patients with a catheter tip colonized with Gram-negative micro-organisms seem to have a relatively high chance of developing a Gram-negative bacteremia. This may be clinically relevant, as starting antibiotic treatment pre-emptively in high-risk patients with Gram-negative micro-organisms cultured from arterial intravenous catheters may be beneficial.

Potential conflicts of interest All authors: no conflicts.

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